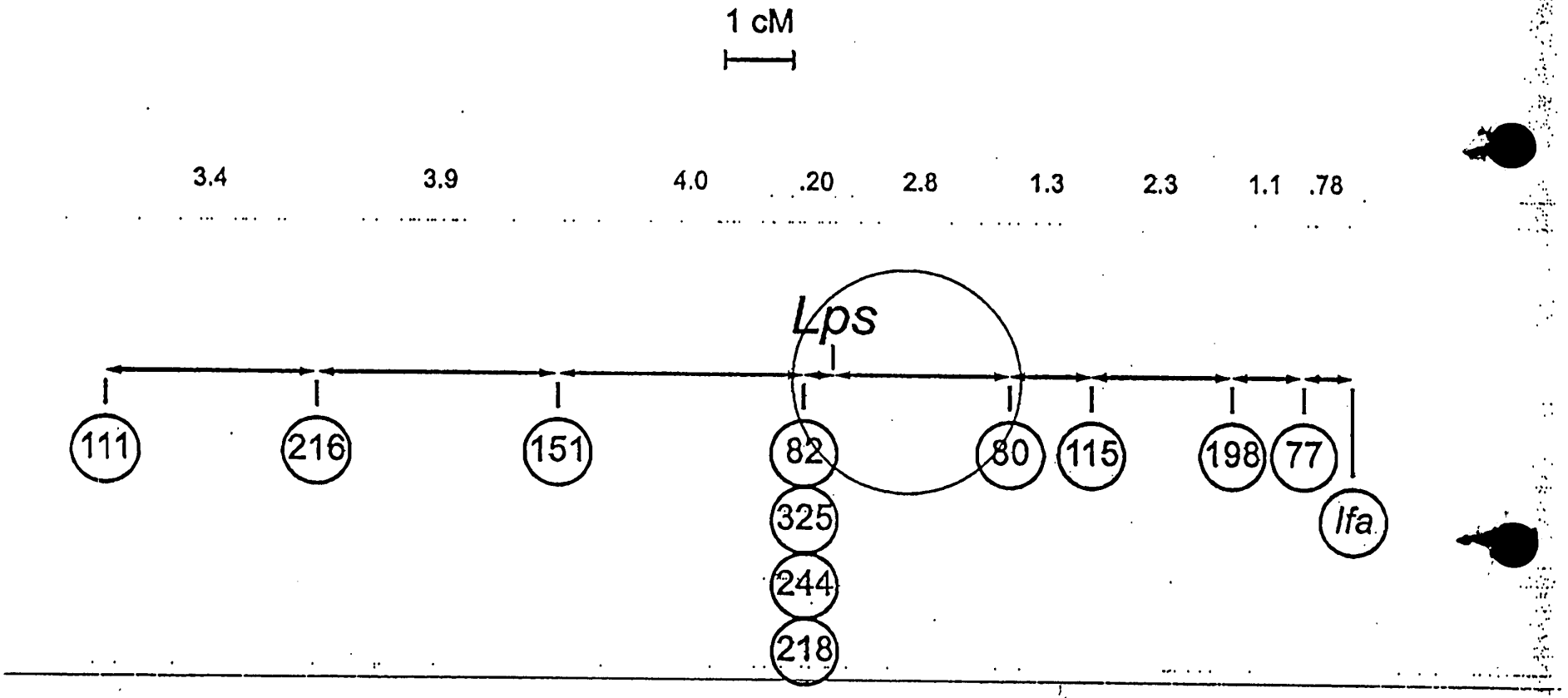


FIG. 1

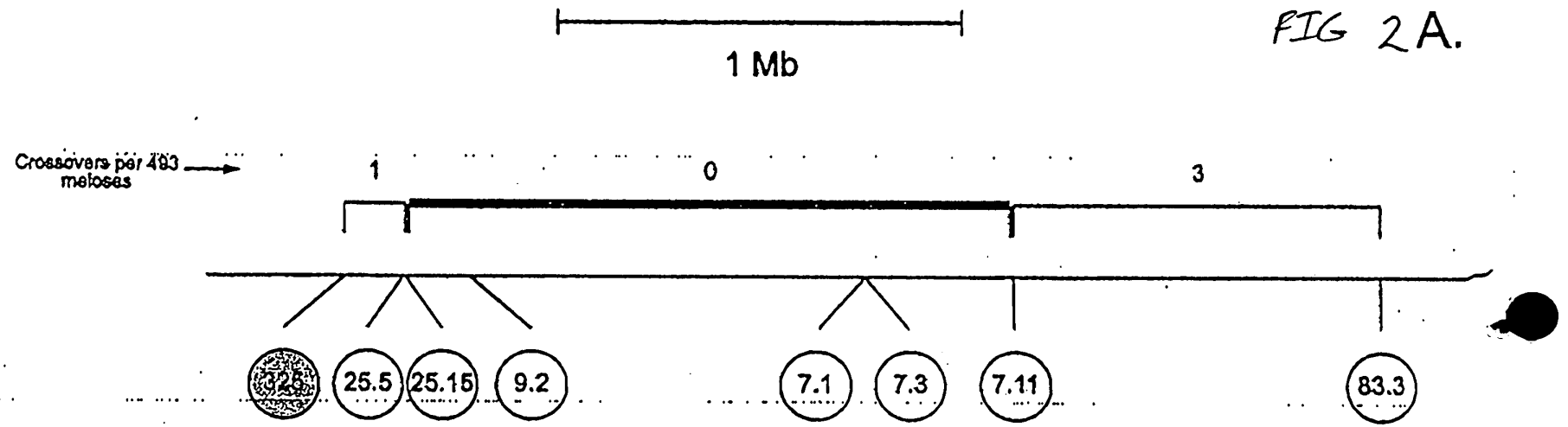


FIG 2A.

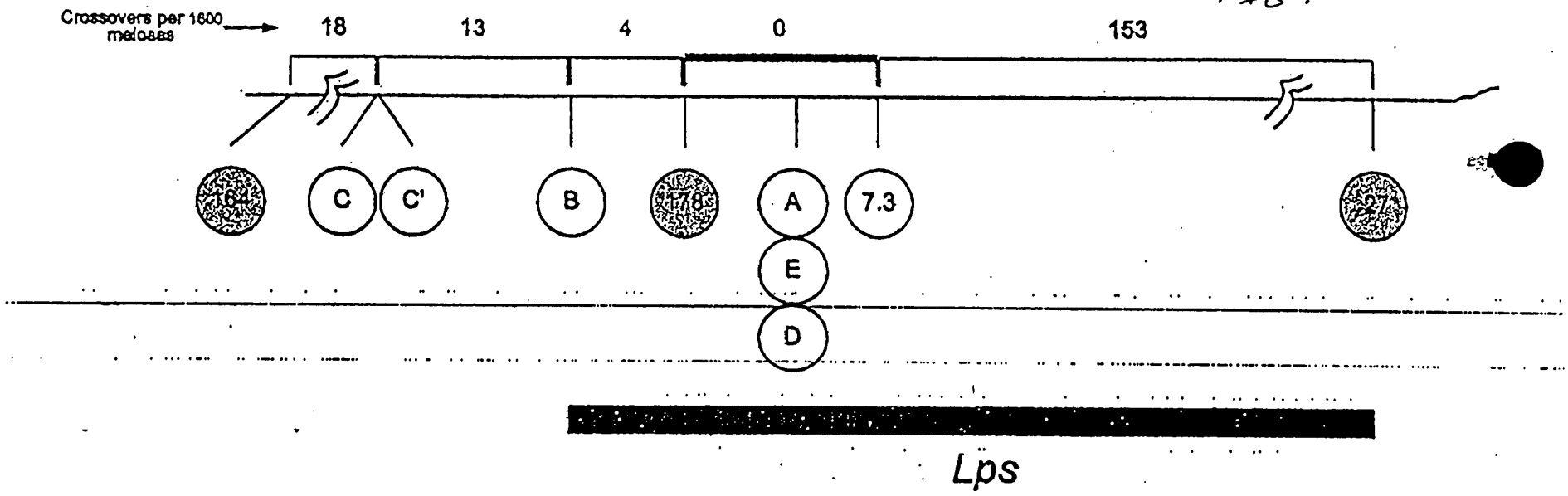


FIG. 2B.

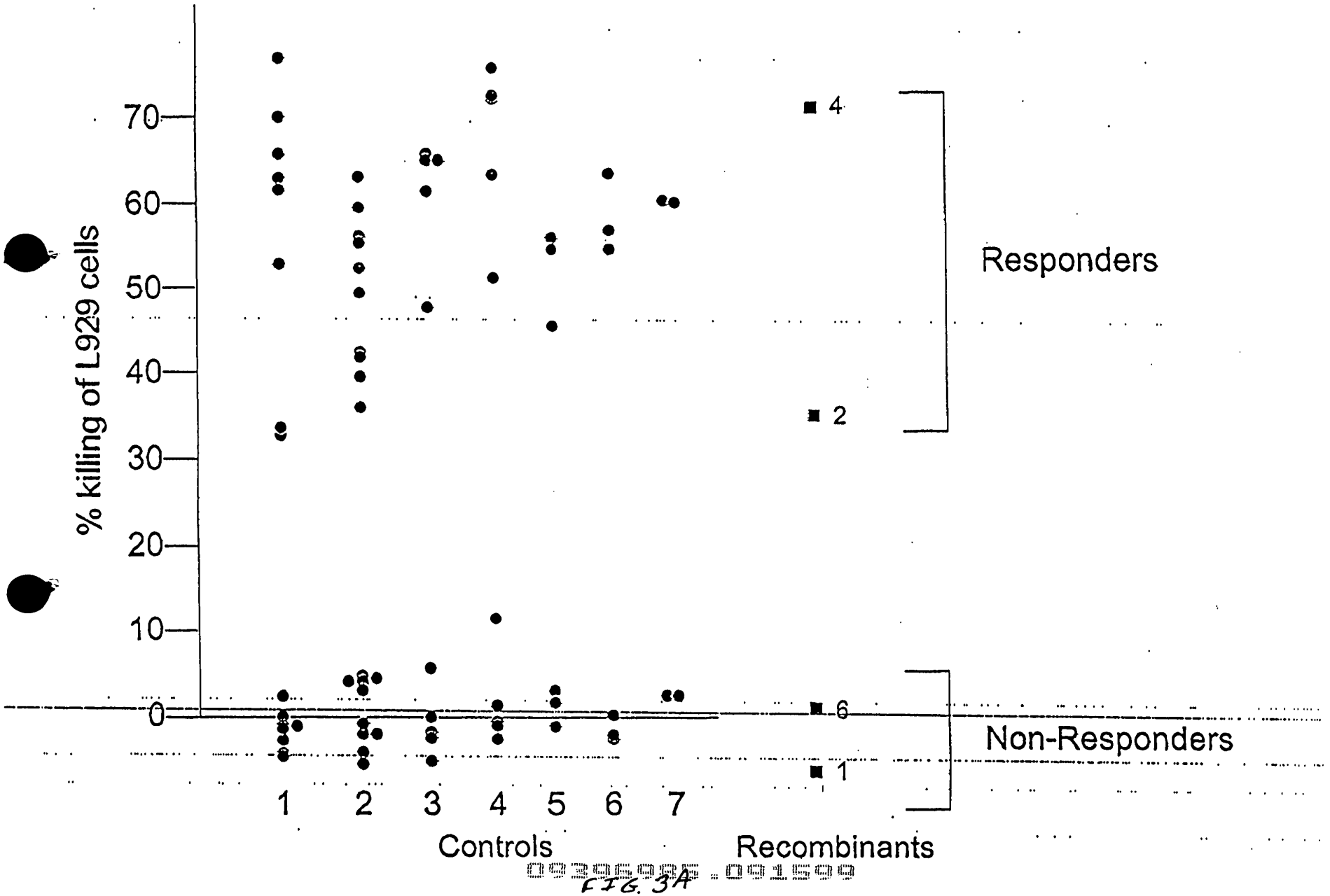
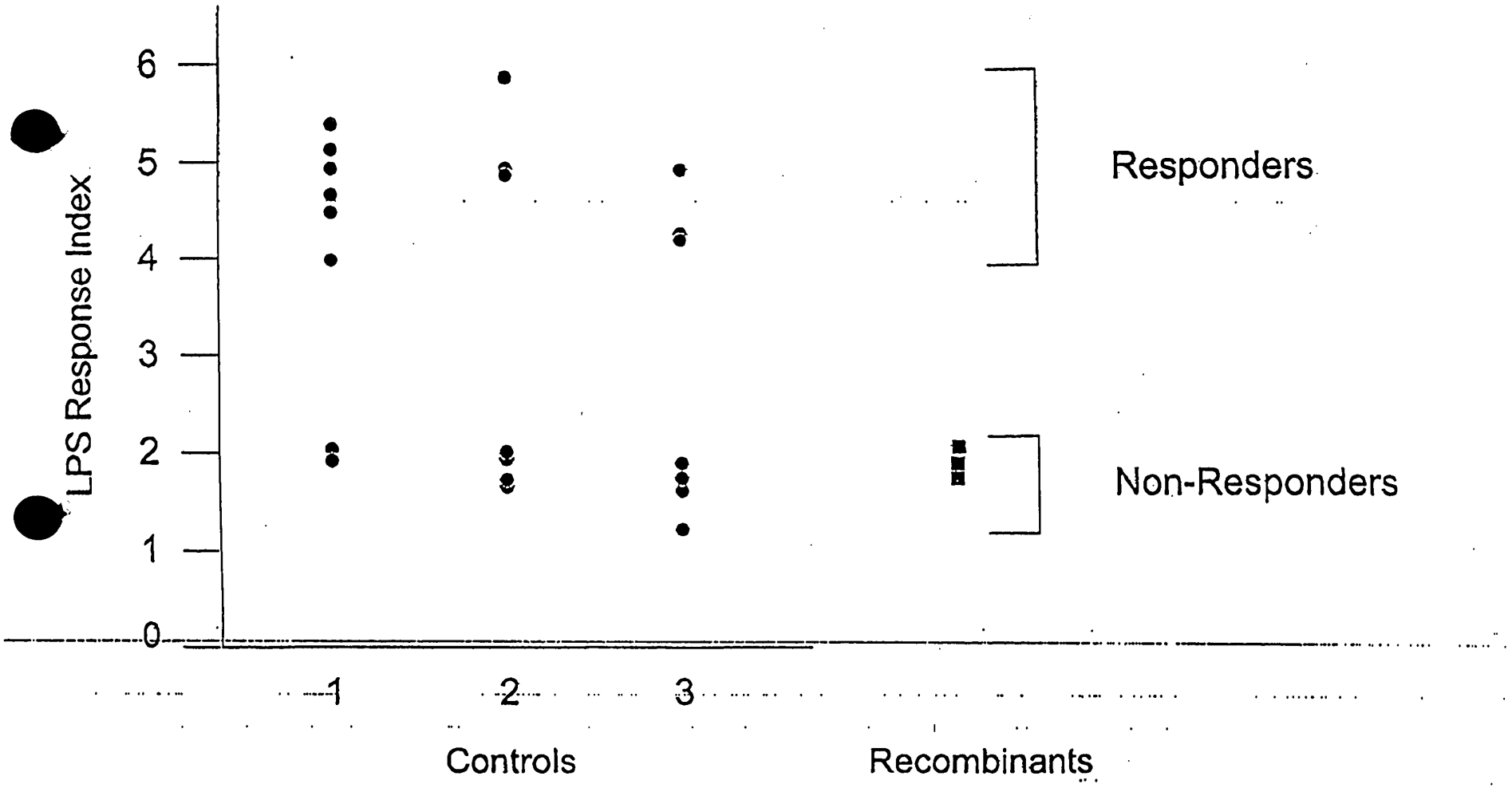

% killing of L929 cells
70
60
50
40
30
20
10
0
1
2
3
4
5
6
7
Controls
Recombinants
Responders
Non-Responders
4
2
6
1

FIG. 3A



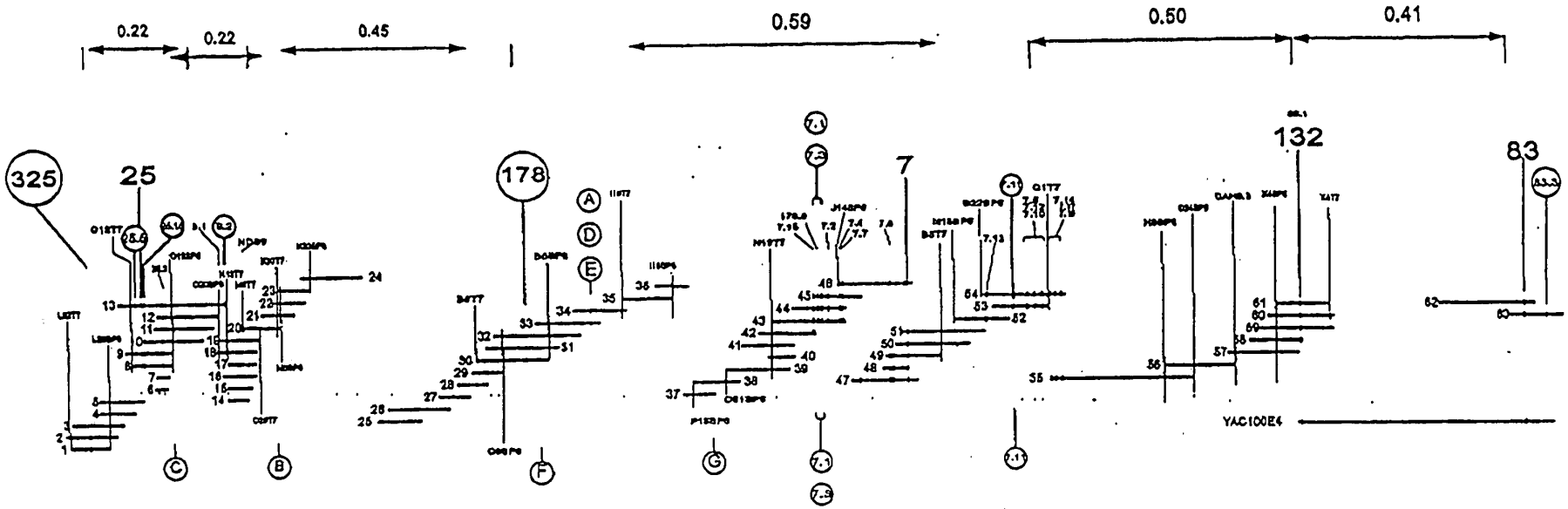


FIG. 4A

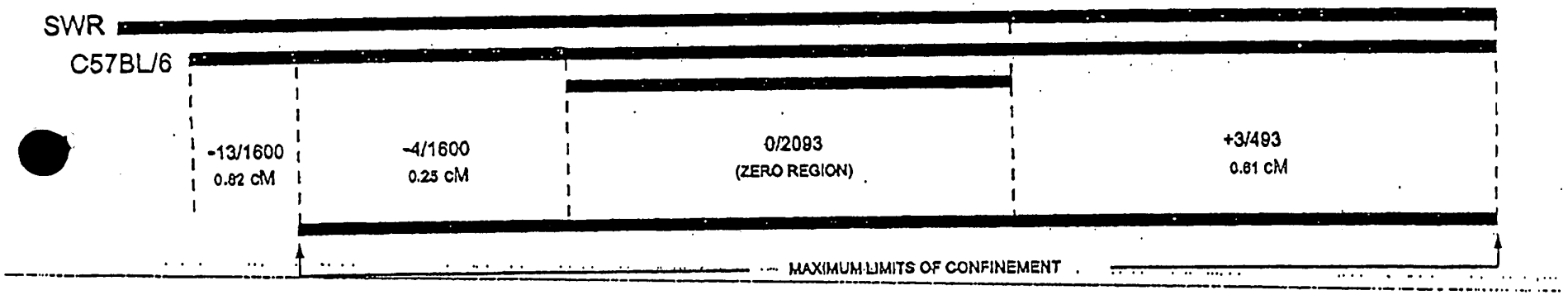
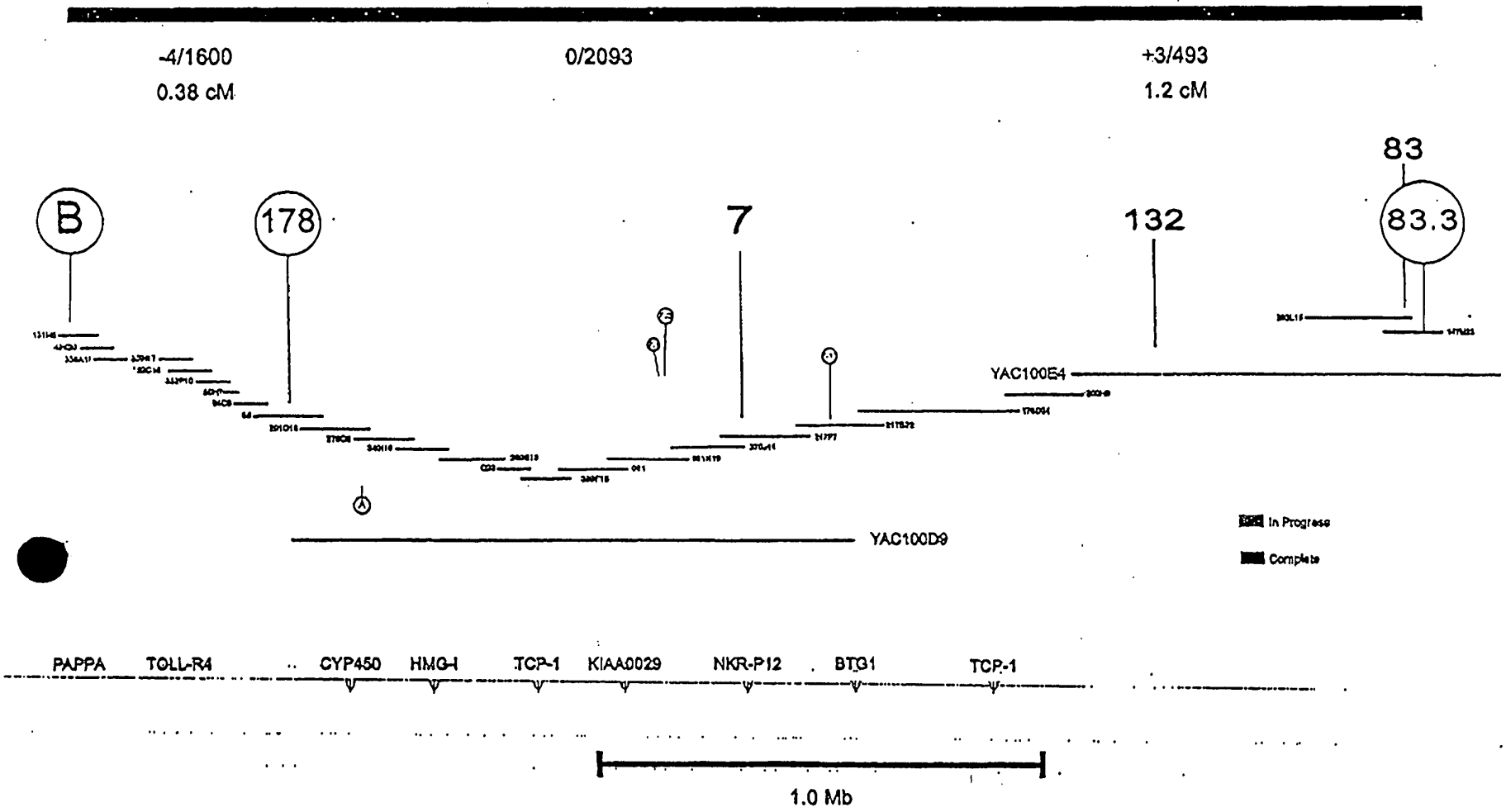


FIG. 4B


-4/1600
0.38 cM
0/2093
+3/493
1.2 cM
B
178
7
132
83
83.3
YAC100E4
YAC100D9
In Progress
Complete
PAPPA
TOLL-R4
CYP450
HMG-I
TCP-1
KIAA0029
NKR-P12
BTG1
TCP-1
1.0 Mb

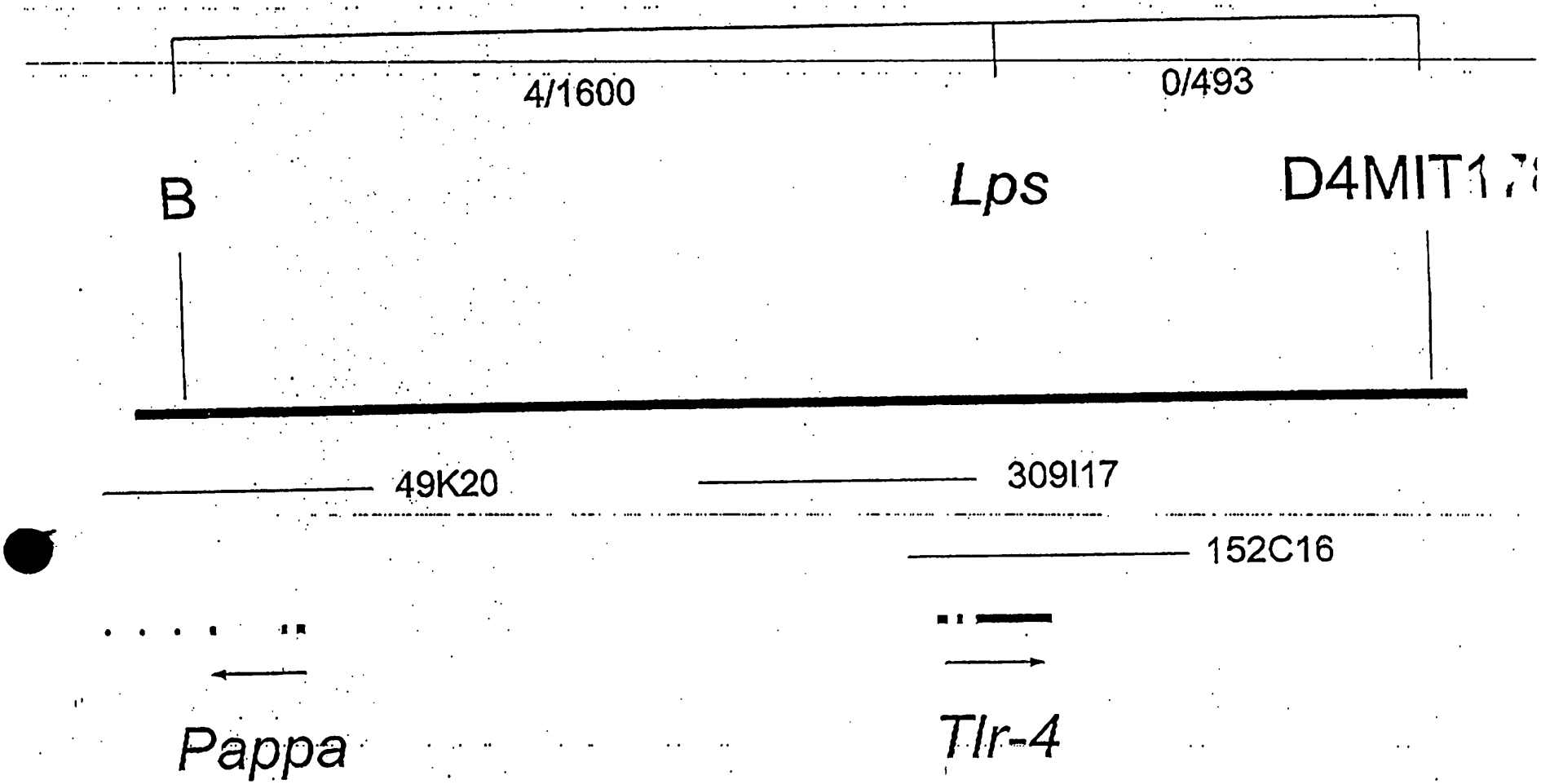


FIG.6

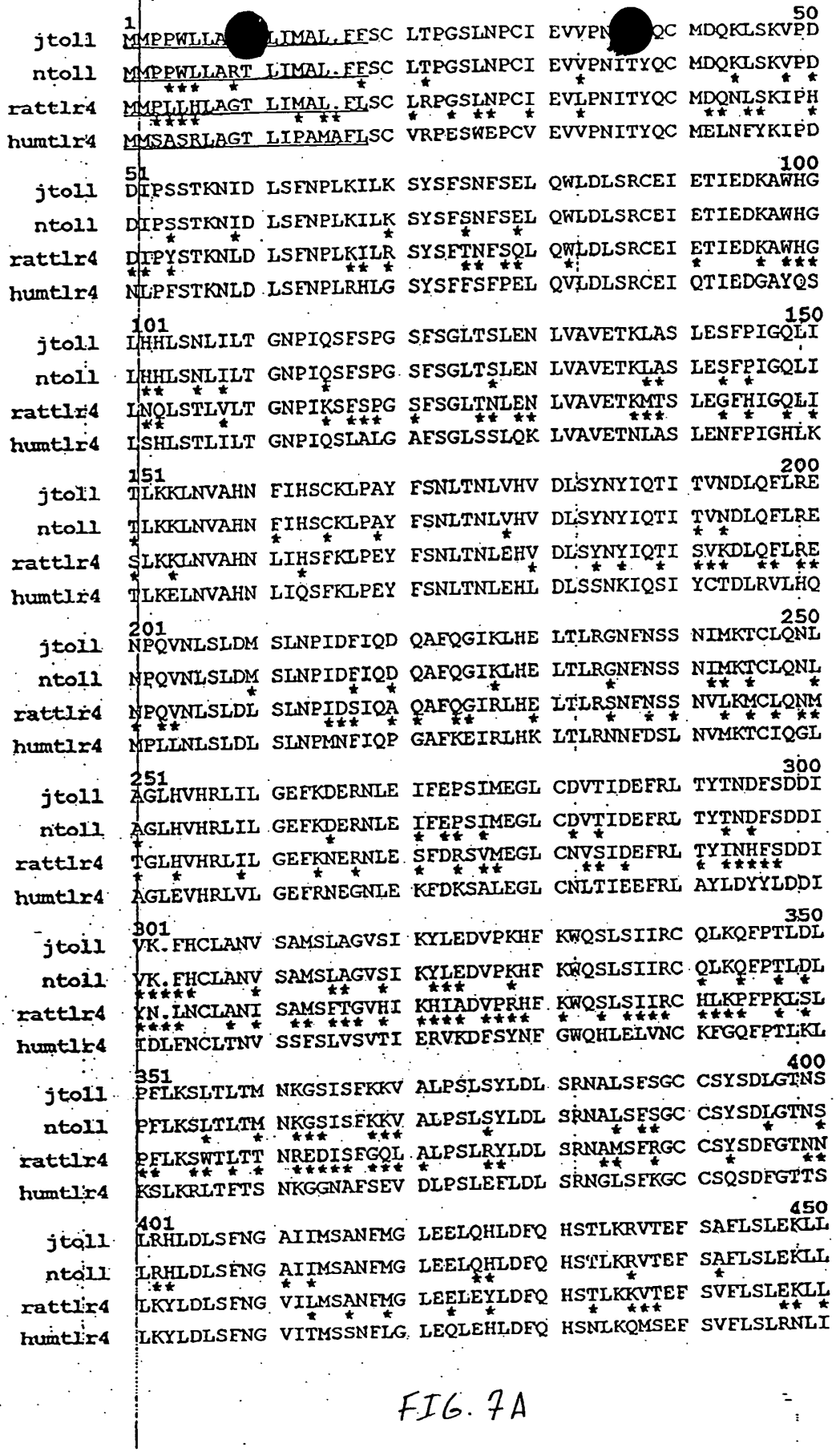

1 50
jtoll MMPPWLLA LIMAL.FFSC LTPGSLNPCI EVVPN QC MDQKLSKVPD
ntoll MMPPWLLART LIMAL.FFSC LTPGSLNPCI EVVPNITYQC MDQKLSKVPD
rattlr4 MMPLLHLAGT LIMAL.FLSC LRPGSLNPCI EVLPNITYQC MDQNLSKIPH
humtlr4 MMSASRLAGT LIPAMAFLSC VRPESWEPCV EVVPNITYQC MELNFYKIPD
51 100
jtoll DIPSSTKNID LSFNPLKILK SYSFSNFSEL QWLDLSRCEI ETIEDKAWHG
ntoll DIPSSTKNID LSFNPLKILK SYSFSNFSEL QWLDLSRCEI ETIEDKAWHG
rattlr4 DIPYSTKNLD LSFNPLKILR SYSFTNFSQL QWLDLSRCEI ETIEDKAWHG
humtlr4 NLPFSTKNLD LSFNPLRHLG SYSFFSFPEL QVLDLSRCEI QTIEDGAYQS
101 150
jtoll LHHLSNLILT GNPIQSFSPG SFSGLTSLEN LVAVETKLAS LESFPIGQLI
ntoll LHHLSNLILT GNPIQSFSPG SFSGLTSLEN LVAVETKLAS LESFPIGQLI
rattlr4 LNQLSTLVLT GNPIKSFSPG SFSGLTNLEN LVAVETKMTS LEGFHIGQLI
humtlr4 LSHLSTLILT GNPIQSLALG AFSGLSSLQK LVAVETNLAS LENFPIGHLK
151 200
jtoll TLKKLNVAHN FIHSCKLPAY FSNLTNLVHV DLSYNYIQTI TVNDLQFLRE
ntoll TLKKLNVAHN FIHSCKLPAY FSNLTNLVHV DLSYNYIQTI TVNDLQFLRE
rattlr4 SLKKLNVAHN LIHSFKLPEY FSNLTNLEHV DLSYNYIQTI SVKDLQFLRE
humtlr4 TLKELNVAHN LIQSFKLPEY FSNLTNLEHL DLSSNKIQSI YCTDLRVLHQ
201 250
jtoll NPQVNLSLDM SLNPIDFIQD QAFQGIKLHE LTLRGNFNSS NIMKTCLQNL
ntoll NPQVNLSLDM SLNPIDFIQD QAFQGIKLHE LTLRGNFNSS NIMKTCLQNL
rattlr4 NPQVNLSLDL SLNPIDSIQA QAFQGIRLHE LTLRSNFNSS NVLKMCLQNM
humtlr4 NPLLNLSLDL SLNPMNFIQP GAFKEIRLHK LTLRNNFDSL NVMKTCIQGL
251 300
jtoll AGLHVHRLIL GEFKDERNLE IFEPSIMEGL CDVTIDEFRL TYTNDFSDDI
ntoll AGLHVHRLIL GEFKDERNLE IFEPSIMEGL CDVTIDEFRL TYTNDFSDDI
rattlr4 TGLHVHRLIL GEFKNERNLE SFDRSVMEGL CNVSIDEFRL TYINHFSDDI
humtlr4 AGLEVHRLVL GEFRNEGNLE KFDKSALEGL CNLTIEEFRL AYLDYYLDDI
301 350
jtoll VK.FHCLANV SAMSLAGVSI KYLEDVPKHF KWQSLSIIRC QLKQFPTLDL
ntoll VK.FHCLANV SAMSLAGVSI KYLEDVPKHF KWQSLSIIRC QLKQFPTLDL
rattlr4 YN.LNCLANI SAMSFTGVHI KHIADVPRHF KWQSLSIIRC HLKPFPKLSL
humtlr4 IDLFNCLTNV SSFSLVSVTI ERVKDFSYNF GWQHLELVNC KFGQFPTLKL
351 400
jtoll PFLKSLTLTM NKGSISFKKV ALPSLSYLDL SRNALSFSGC CSYSDLGTNS
ntoll PFLKSLTLTM NKGSISFKKV ALPSLSYLDL SRNALSFSGC CSYSDLGTNS
rattlr4 PFLKSWTLTT NREDISFGQL ALPSLRYLDL SRNAMSFRGC CSYSDFGTNN
humtlr4 KSLKRLTFTS NKGGNAFSEV DLPSLEFLDL SRNGLSFKGC CSQSDFGTTS
401 450
jtoll LRHLDLSFNG AIIMSANFMG LEELQHLDFQ HSTLKRVTEF SAFLSLEKLL
ntoll LRHLDLSFNG AIIMSANFMG LEELQHLDFQ HSTLKRVTEF SAFLSLEKLL
rattlr4 LKYLDLSFNG VILMSANFMG LEELEYLDFQ HSTLKKVTEF SVFLSLEKLL
humtlr4 LKYLDLSFNG VITMSSNFLG LEQLEHLDFQ HSNLKQMSEF SVFLSLRNLI

FIG. 7A

```
          451                                                      500
jtoll     YLDISYTNTK IDFDGIFLGL TSLNTLKMAG NSFKDNTLSN VFANTTNLTF
ntoll     YLDISYTNTK IDFDGIFLGL TSLNTLKMAG NSFKDNTLSN VFANTTNLTF
                                *
rattlr4   YLDISYTNTK IDFDGIFLGL ISLNTLKMAG NSFKDNTLSN VFTNTTNLTF
              * * *   ** *    *   *  **        ** *  **  *   ***
humtlr4   YLDISHTHTR VAFNGIFNGL SSLEVLKMAG NSFQENFLPD IFTELRNLTF

          501                                                      550
jtoll     LDLSKCQLEQ ISWGVFDTLH RLQLLNMSHN NLLFLDSSHY NQLYSLSTLD
ntoll     LDLSKCQLEQ ISWGVFDTLH RLQLLNMSHN NLLFLDSSHY NQLYSLSTLD
                        *       **                  *       *    *
rattlr4   LDLSKCQLEQ ISRGVFDTLY RLQLLNMSHN NLLFLDPSHY KQLYSLRTLD
              *       * ***  ** *  *  *      ***  ***    * *  **
humtlr4   LDLSQCQLEQ LSPTAFNSLS SLQVLNMSHN NFFSLDTFPY KCLNSLQVLD

          551                                                      600
jtoll     CSFNRIETS. KGILQHFPKS LAFFNLTNNS VACICEHQKF LQWVKEQKQF
ntoll     CSFNRIETS. KGILQHFPKS LAFFNLTNNS VACICEHQKF LQWVKEQKQF
                                  *              * *        *  *
rattlr4   CSFNRIETS. KGILQHFPKS LAVFNLTNNS VACICEYQNF LQWVKDQKMF
          * * * *  *   **     *    **   *  *   *   *  *   *    ***
humtlr4   YSLNHIMTSK KQELQHFPSS LAFLNLTQND FACTCEHQSF LQWIKDQRQL

          601                                                      650
jtoll     LVNVEQMTCA TPVEMNTSLV LDFNNSTCYM YKTIISVSVV SVIVVSTVAF
ntoll     LVNVEQMTCA TPVEMNTSLV LDFNNSTCYM YKTIISVSVV SVIVVSTVAF
                  *   * ** **        *      *                *   *
rattlr4   LVNVEQMKCA SPIDMKASLV LDFTNSTCYI YKTIISVSVV SVLVVATVAF
            *   *   *   * * *****  ***  *  ** *                **  *
humtlr4   LVEVERMECA TPSDKQGMPV LSL.NITCQM NKTIIGVSVL SVLVVSVVAV

          651                                                      700
jtoll     LIYHFYFHLI LIAGCKKYSR GESIYDAFVI YSSQNEDWVR NELVKNLEEG
ntoll     LIYHFYFHLI LIAGCKKYSR GESIYDAFVI YSSQNEDWVR NELVKNLEEG
rattlr4   LIYHFYFHLI LIAGCKKYSR GESIYDAFVI YSSQNEDWVR NELVKNLEEG
            * *     *  *    *  *    *          *
humtlr4   LVYKFYFHLM LLAGCIKYGR GENIYDAFVI YSSQDEDWVR NELVKNLEEG

          701                                                      750
jtoll     VPRFHLCLHY RDFIHGVAIA ANIIQEGFHK SRKVIVVVSR HFIQSRWCIF
                        *
ntoll     VPRFHLCLHY RDFIPGVAIA ANIIQEGFHK SRKVIVVVSR HFIQSRWCIF
              *
rattlr4   VPRFQLCLHY RDFIPGVAIA ANIIQEGFHK SRKVIVVVSR HFIQSRWCIF
            *                       *                 *
humtlr4   VPPFQLCLHY RDFIPGVAIA ANIIHEGFHK SRKVIVVVSQ HFIQSRWCIF

          751                                                      800
jtoll     EYEIAQTWQF LSSRSGIIFI VLEKVEKSLL RQQVELYRLL SRNTYLEWED
ntoll     EYEIAQTWQF LSSRSGIIFI VLEKVEKSLL RQQVELYRLL SRNTYLEWED
rattlr4   EYEIAQTWQF LSSRSGIIFI VLEKVEKSLL RQQVELYRLL SRNTYLEWED
                         *         *    *
humtlr4   EYEIAQTWQF LSSRAGIIFI VLQKVEKTLL RQQVELYRLL SRNTYLEWED

          801                                 840
jtoll     NPLGRHIFWR RLKNALLDGK ASNPEQTAEE EQETATWT~~
ntoll     NPLGRHIFWR RLKNALLDGK ASNPEQTAEE EQETATWT~~
           *           *        *  ** *        *
rattlr4   NALGRHIFWR RLKKALLDGK ALNPDETSEE EQEATTLT~~
          **            *       **  ** ***  *******
humtlr4   SVLGRHIFWR RLRKALLDGK SWNPEGTVGT GCNWQEATSI
```

FIG. 7A (cont.)

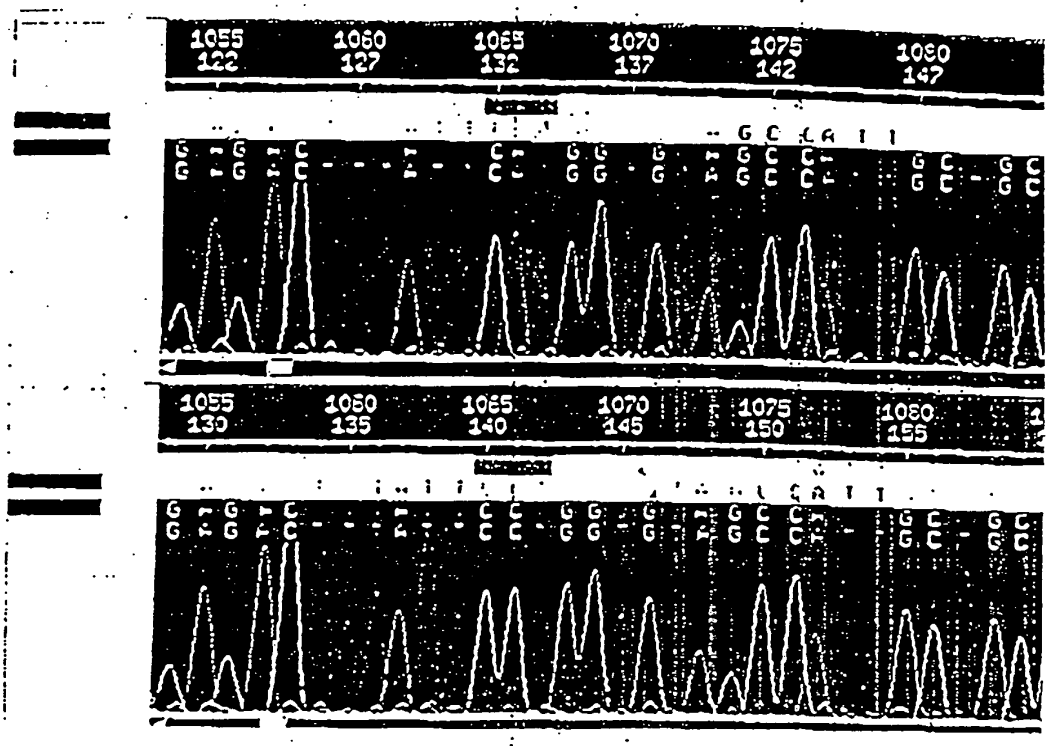

1055
122
1060
127
1065
132
1070
137
1075
142
1080
147
1055
130
1060
135
1065
140
1070
145
1075
150
1080
155

FIG. 7B

FIG. 8A

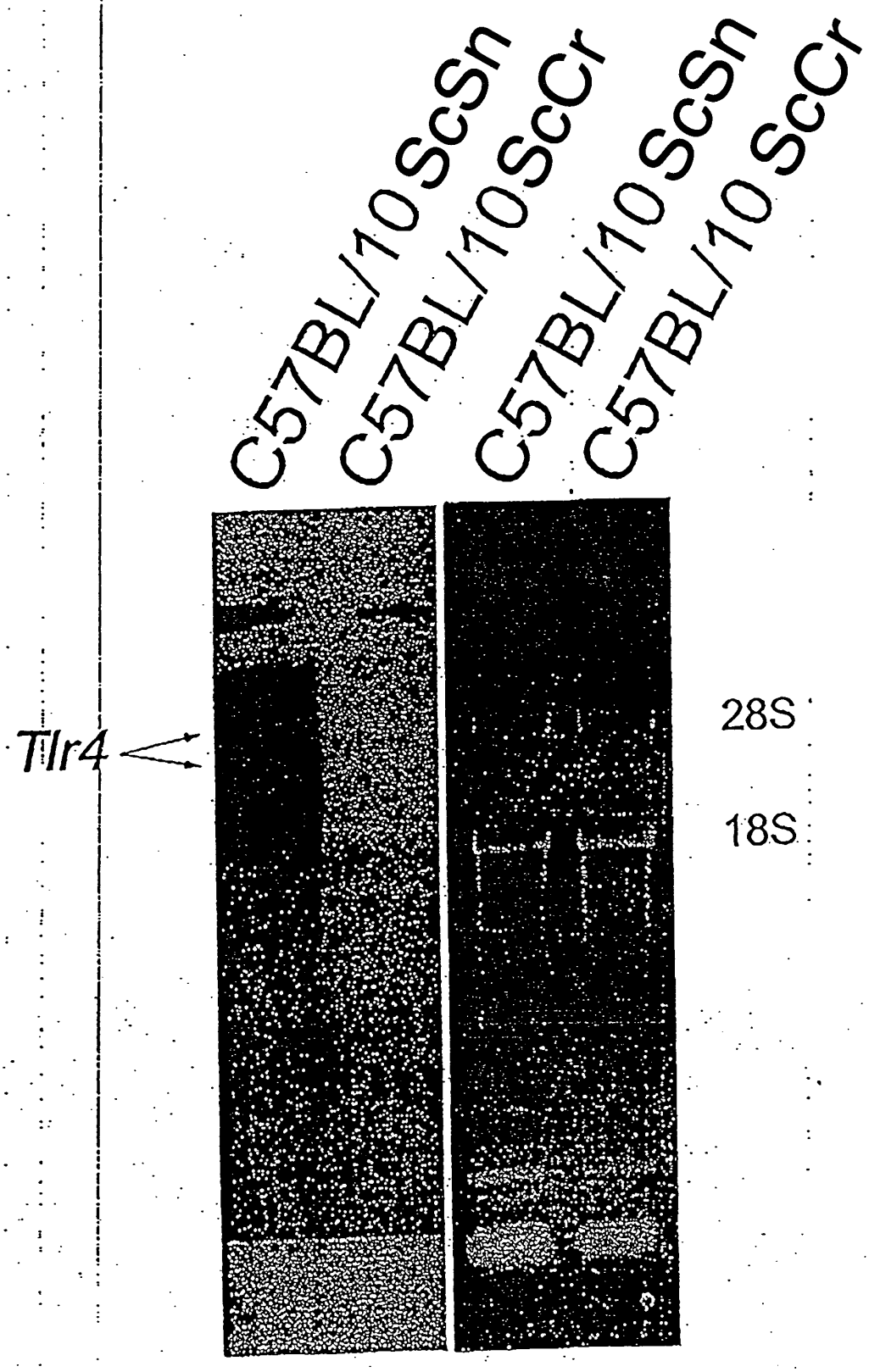

C57BL/10ScSn
C57BL/10ScCr
C57BL/10ScSn
C57BL/10ScCr
Tlr4
28S
18S

FIG. 8B

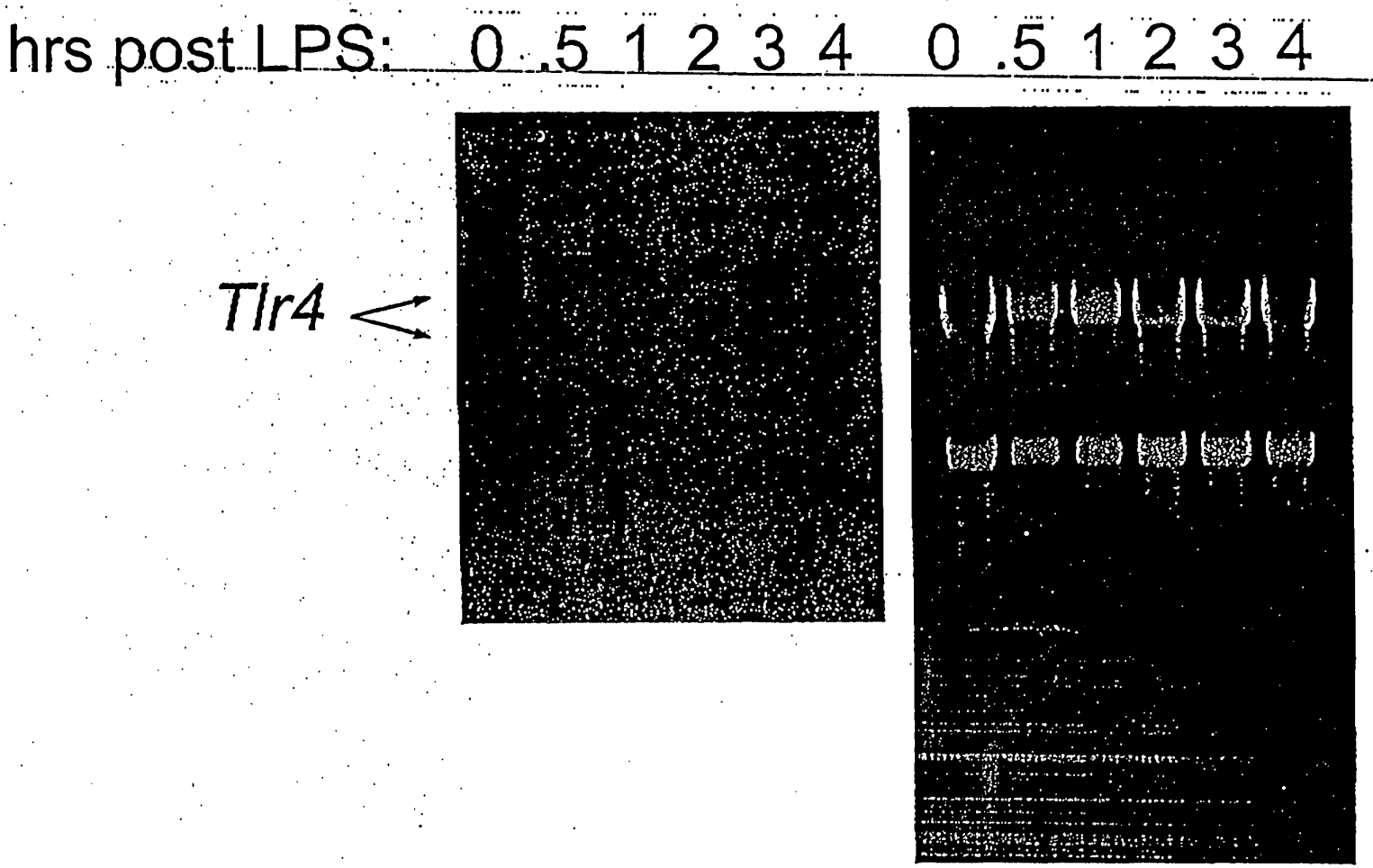


FIG. 9

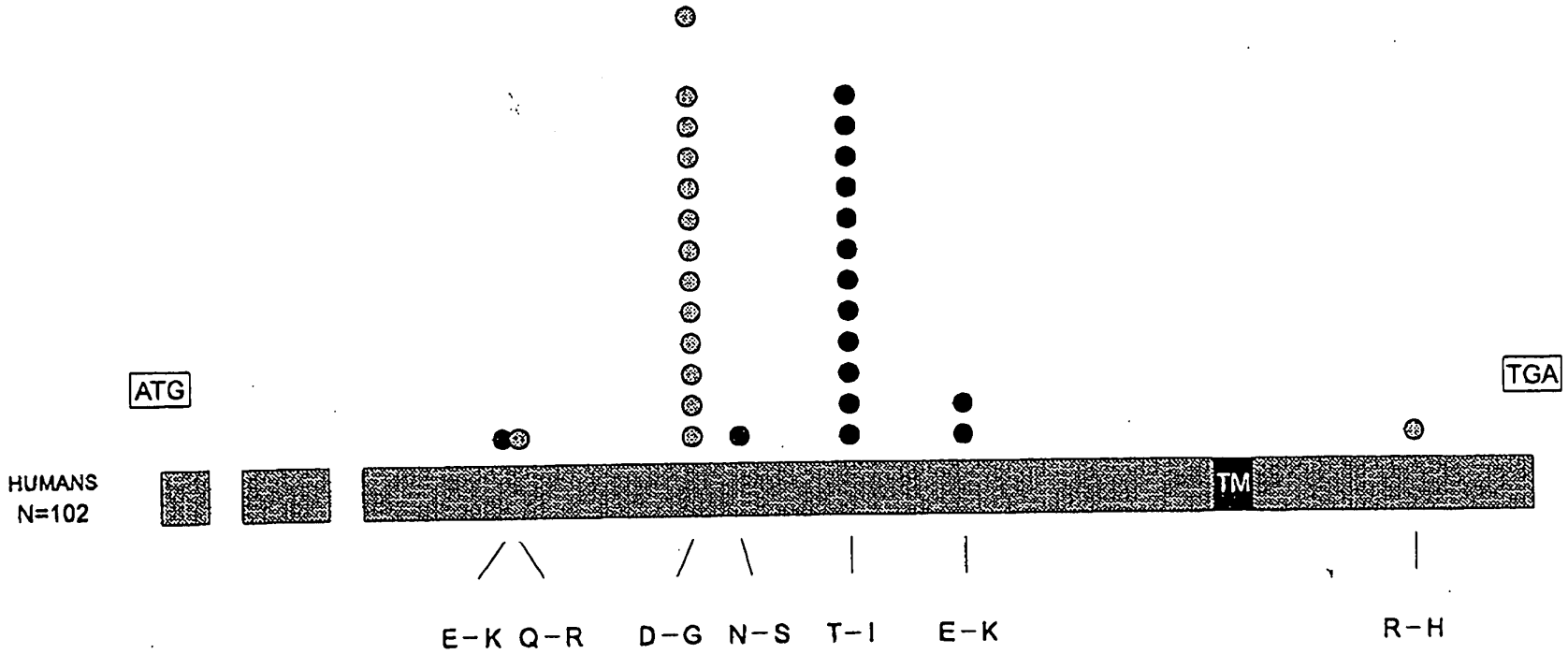


FIG. 10

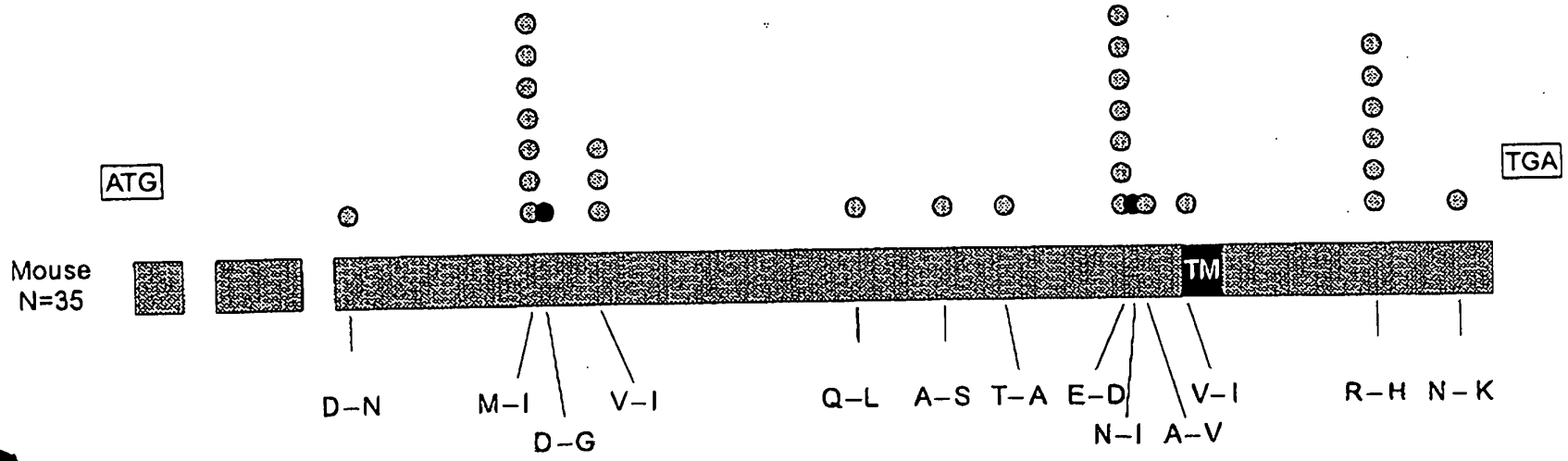


FIG. 11

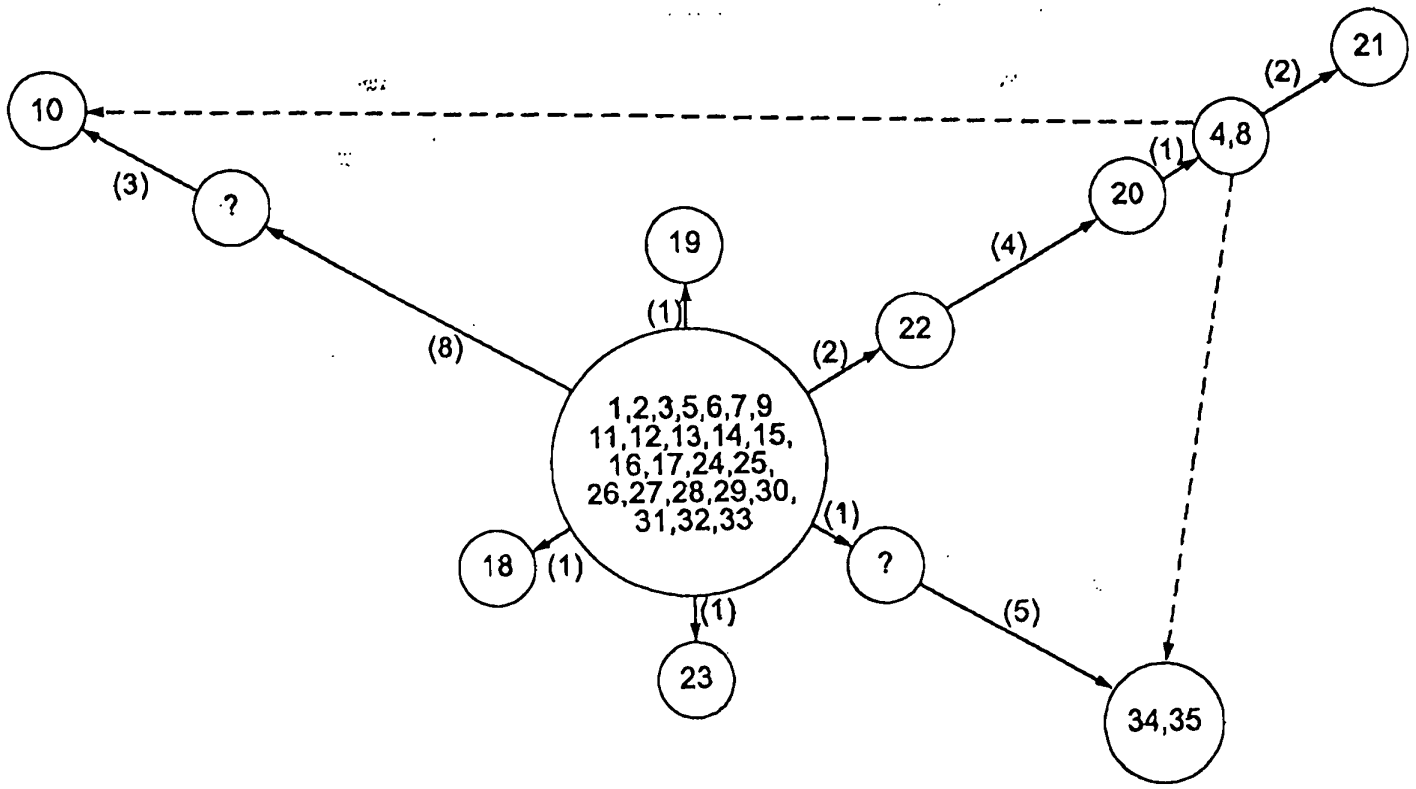

10
(3)
?
(8)
19
(1)
1,2,3,5,6,7,9
11,12,13,14,15,
16,17,24,25,
26,27,28,29,30,
31,32,33
18
(1)
(1)
23
(2)
22
(4)
20
(1)
4,8
(2)
21
(1)
?
(5)
34,35

FIG. 12

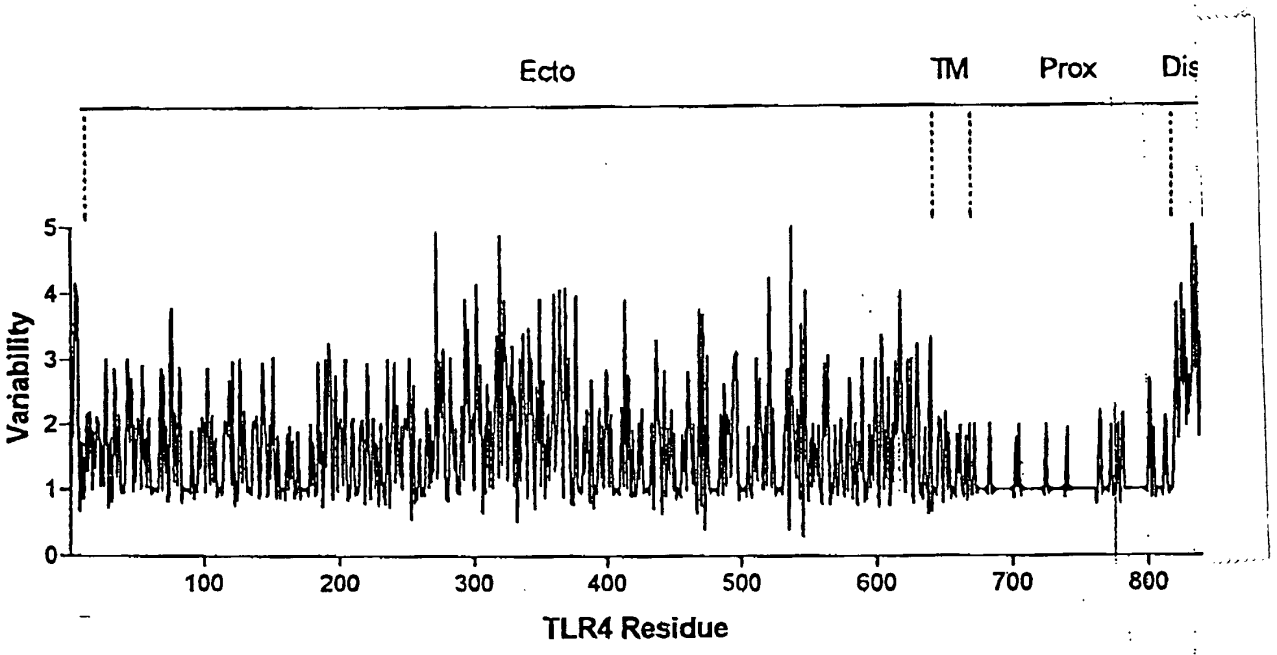

Ecto
TM
Prox
Dis
Variability
0
1
2
3
4
5
100
200
300
400
500
600
700
800
TLR4 Residue

FIG. 13

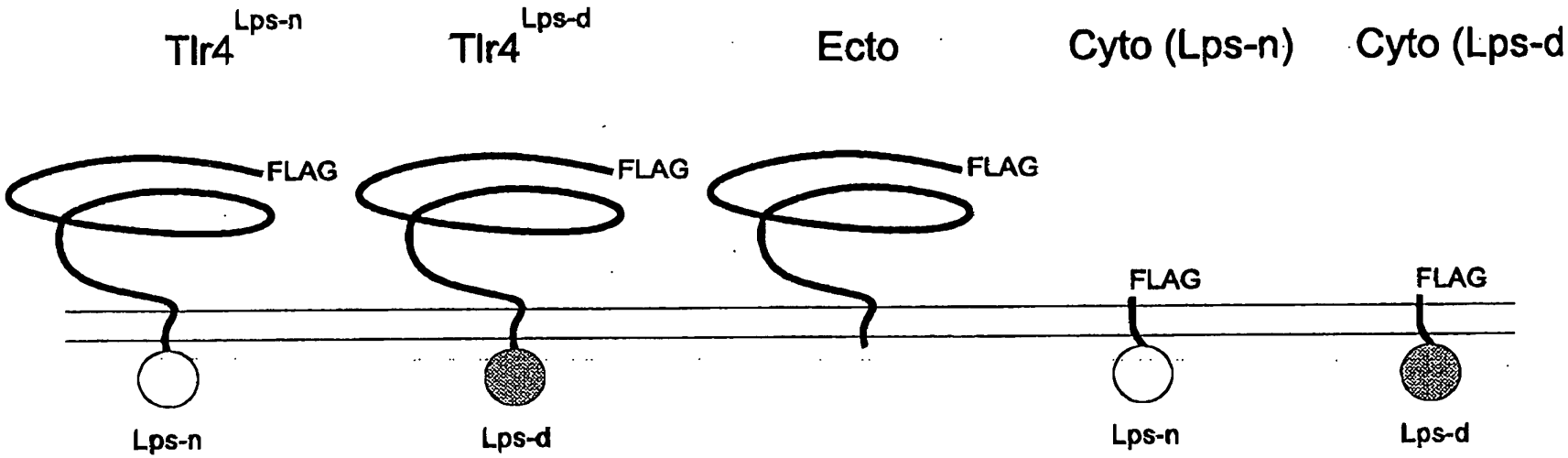


FIG. 14

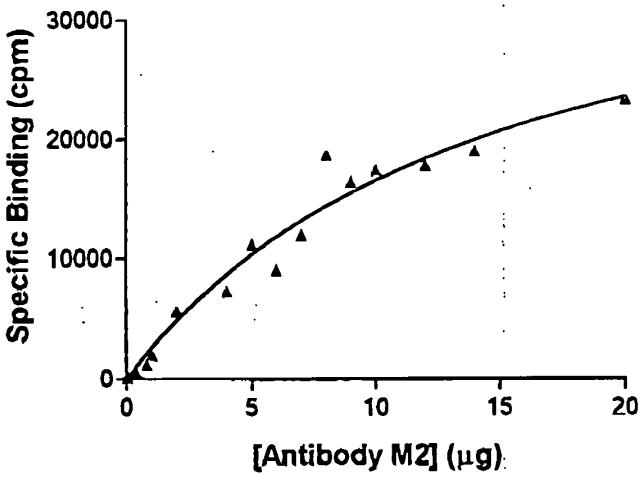

Specific Binding (cpm)
30000
20000
10000
0
0
5
10
15
20
[Antibody M2] (µg)

FIG. 15A

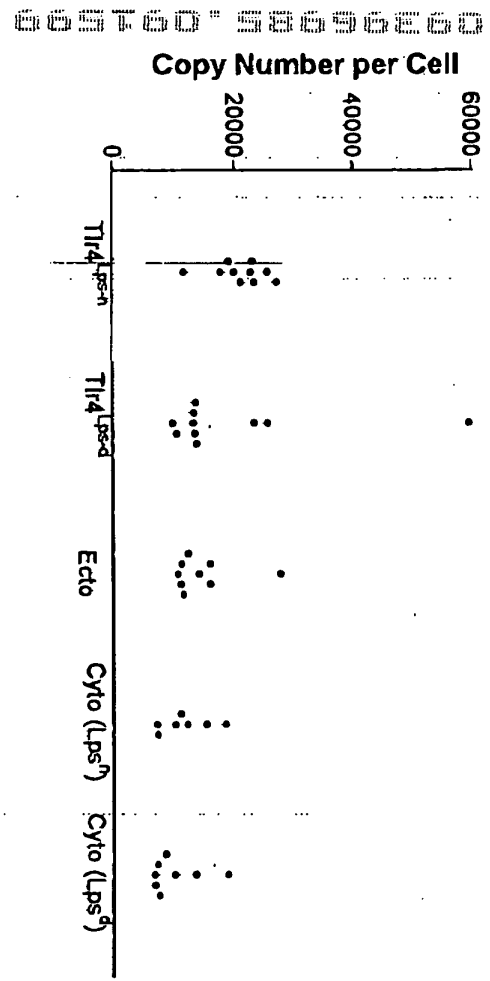

Copy Number per Cell
0
20000
40000
60000
Tlr4Lps-n
Tlr4Lps-d
Ecto
Cyto (Lps^n)
Cyto (Lps^d)

FIG. 15B

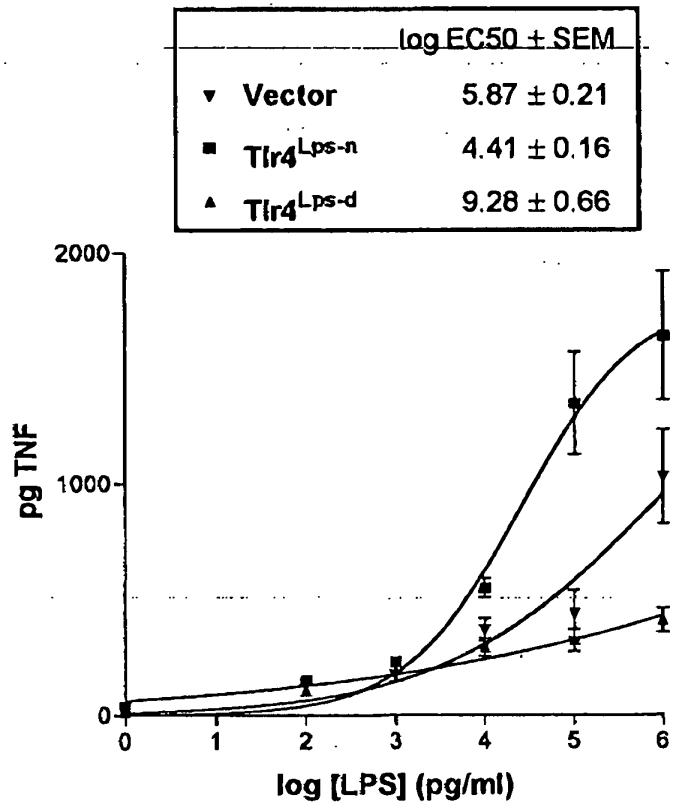


FIG. 15C

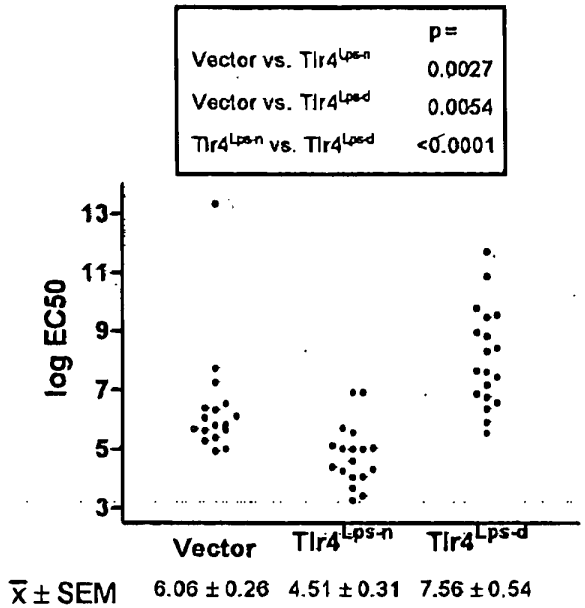


FIG. 15D

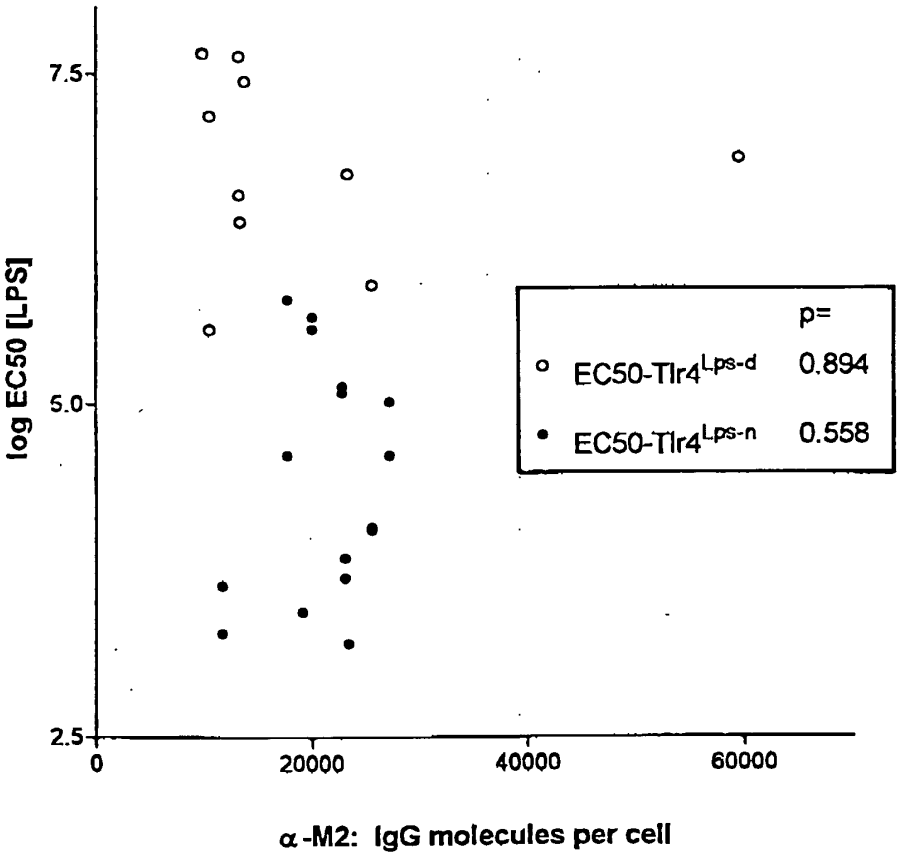

7.5
5.0
2.5
log EC50 [LPS]
0
20000
40000
60000
α-M2: IgG molecules per cell
p=
EC50-Tlr4Lps-d 0.894
EC50-Tlr4Lps-n 0.558

FIG. 15E

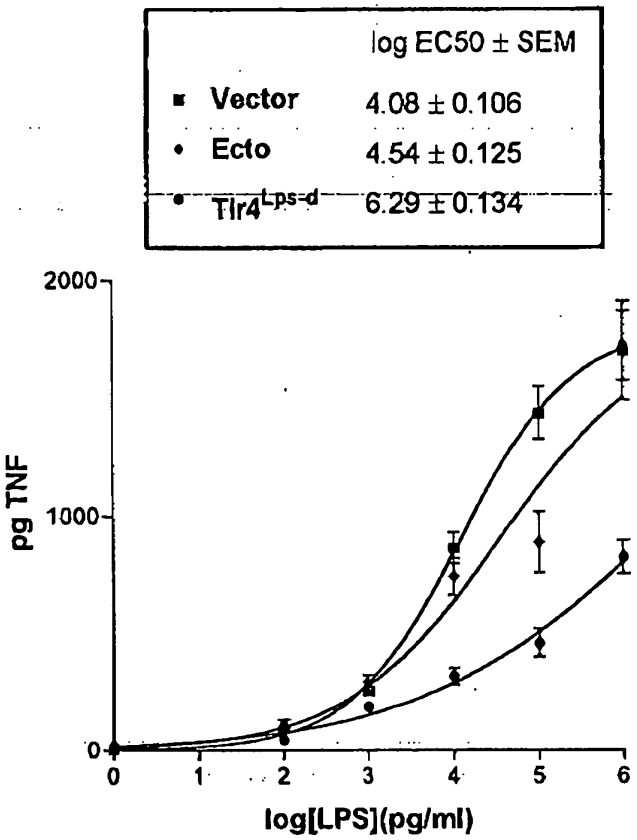


FIG. 16A

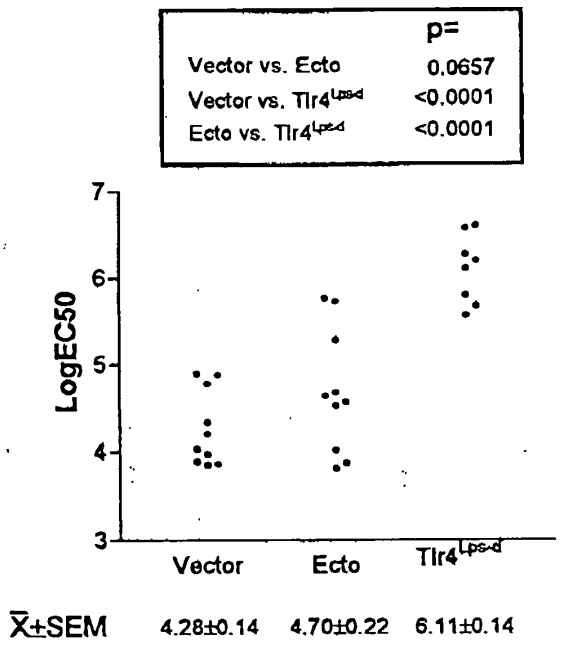

p=
Vector vs. Ecto 0.0657
Vector vs. Tlr4Lps-d <0.0001
Ecto vs. Tlr4Lps-d <0.0001
LogEC50
7
6
5
4
3
Vector
Ecto
Tlr4Lps-d
X̄±SEM
4.28±0.14
4.70±0.22
6.11±0.14

FIG. 16B

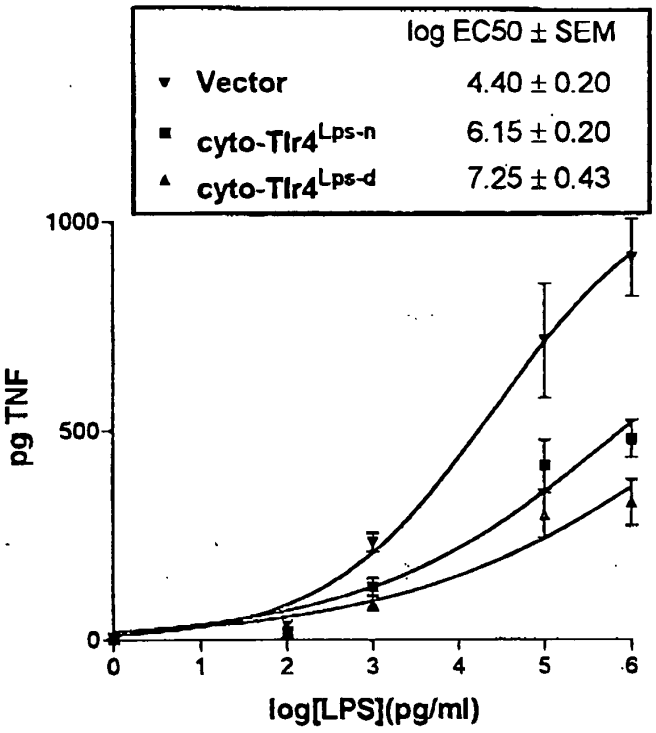

log EC50 ± SEM
Vector 4.40 ± 0.20
cyto-Tlr4Lps-n 6.15 ± 0.20
cyto-Tlr4Lps-d 7.25 ± 0.43
pg TNF
1000
500
0
0
1
2
3
4
5
6
log[LPS](pg/ml)

FIG. 17A

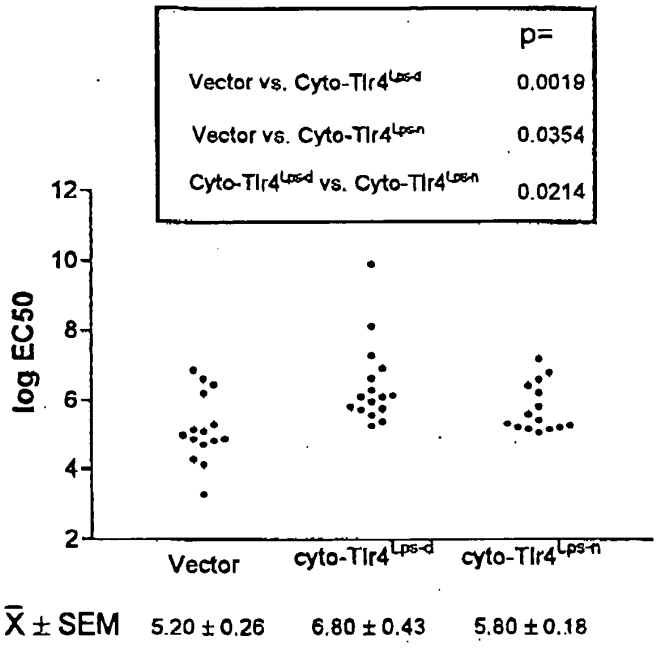

p=
Vector vs. Cyto-Tlr4Lps-d 0.0018
Vector vs. Cyto-Tlr4Lps-n 0.0354
Cyto-Tlr4Lps-d vs. Cyto-Tlr4Lps-n 0.0214
log EC50
12
10
8
6
4
2
Vector
cyto-Tlr4Lps-d
cyto-Tlr4Lps-n
X̄ ± SEM 5.20 ± 0.26 6.80 ± 0.43 5.80 ± 0.18

FIG. 17B